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Hemostatic Profile of Normal Pregnant Women in Gaza strip

عوامل التجلط في النساء الحوامل طبيعيا في قطاع غزة

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إقـــــرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان:

Hemostatic Profile of Normal Pregnant Women in Gaza strip

عوامل التجلط في النساء الحوامل طبيعيا في قطاع غزة

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Abstract

Background: Normal pregnancy has been associated with alteration of the hemostatic system. Pregnancy is recognized as a hypercoagulable state that protect women from potentially hemorrhage during placentation and the post-partum period.

Objective: To assess hemostatic profile of normal pregnant women in Gaza strip.

Materials and methods: This case-control design study included 105 healthy pregnant women subdivided into three groups each consists of 35 women comprising 1st, 2nd and 3rd trimesters, and 35 healthy non-pregnant women. Questionnaire interviews were applied. Hemostatic profiles were assessed. Data were computer analyzed using SPSS program version 21.

Results: The mean ages of controls and pregnant women in the first, second and third trimesters were 29.0±5.1, 28.6±6.2, 28.7±5.8 and 28.9±6.1 years old, respectively. Unemployment women and lower family income were more prevalent among pregnant women (P=0.004 and P=0.002, respectively). Diastolic blood pressure recorded significant decrease in pregnant women compared to non-pregnant women (P=0.031). PT and INR were significantly decreased as pregnancy progress (P=0.001). Conversely, fibrinogen was significantly elevated in the 1st, 2nd and 3rd trimesters compared to controls (P=0.001). RBCs count, Hb, platelets count, lymphocytes count and Ca concentration showed significant decrease in the three trimesters of pregnancy compared to controls (P=0.001, P=0.001, P=0.001, P=0.001 and P=0.003, respectively). Whereas there were significant increases in the means of WBCs count, MID cells, granulocytes count and ESR in the three trimesters of pregnancy compared to controls (P=0.002 for WBC; P=0.030 for MID cells, P=0.001 for granulocyte and P=0.001 for ESR). Similarly there was significant increase in MCV in the 3rd trimester compared to the 1s trimester (P=0.006). MCHC displays significant increases in the 1st trimester with respect to controls and then significant decreases was recorded in the 2nd and 3rd trimesters compared to 1st trimester (P=0.001). The Pearson correlation coefficient test showed significant positive correlations of fibrinogen with WBC (r=0.196, P=0.045), Granulocyte (r=0.219, P=0.025) and ESR (r=0.260, P=0.007) in pregnant women.

Conclusions: Hemostatic parameters were altered during pregnancy. There were significantly increases in fibrinogen, WBC, MID, granulocytes, MCV and ESR during pregnancy. In contrast PT, INR , lymphocytes, RBC, Hb, Hct, MCHC, platelets and calcium were significantly deceased. Fibrinogen showed significant positive correlations with WBC, granulocyte and ESR.

Arabic abstract

خلفية البحث: يرتبط الحمل الطبيعي عادة مع تغيير في نظام وقف نزيف الدم. ويعرف الحمل كحالة مفرطة الخثورية التي تحمي المرأة من النزف المحتمل من خلال المشيمة وفي فترة ما بعد الولادة.

هدف الدراسة: تقييم حالات وقف نزيف الدم عند النساء الحوامل طبيعيا في قطاع غزة.

المواد والمنهجية: تضمنت هذه الدراسة تصميم دراسة الحالات الإفرادية المقترنة بحالات ضابطة ل ١٠٥ امرأة حامل وبصحة جيدة تم تقسيمهن إلى ثلاث مجموعات كل واحدة تتكون من ٣٥ امرأة في الثلث الاول والثاني والثالث من الحمل ثم ٣٥ امرأة سليمة غير حامل كمجموعة ضابطة. وقد تم تطبيق الاستبيان والمقابلات وتم تقييم الحلات الشخصية لوقف نزيف الدم. وتم تحليل البيانات باستخدام برنامج SPSS النسخة ٢١.

النتائج: كانت متوسط أعمار النساء في المجموعة الضابطة ومجموعات النساء الحوامل في الثلث الأول والثاني والثالث من الحمل هي ٢٩.٠ ± ٥.١، ٢٨.٦ ± ٦.٢، ٢٨.٧ ± ٥.٨ و٢٨.٩ ± ٦.١ سنة، على التوالي. شكلت النساء غير العاملات وذوات دخل الأسرة المنخفض الأكثر عدداً بين النساء الحوامل (P= 0.004 و P= 0.002 على التوالي). سجل ضغط الدم الانبساطي انخفاض ملحوظا عند النساء الحوامل مقارنة بالنساء غير الحوامل (P = 0.031). قل كلا من ال PT وINR بشكل ملحوظ كلما تقدم الحمل (P = 0.001). على العكس من ذلك، كان الفيبرينوجين مرتفعا إلى حد كبير في مجموعات الثلث الثاني والثالث مقارنة مع المجموعة الضابطة (P= 0.001). وأظهر عدد كرات الدم الحمراء، والهيموغلوبين، وعدد الصفائح الدموية، وعدد الخلايا الليمفاوية وتركيز الكالسيوم انخفاضا كبيرا في مجموعة الثلث الثالث من الحمل مقارنة مع المجموعة الضابطة (P = 0.001، P = 0.001، P = 0.001، P = 0.001 و P = 0.003 على التوالي). بينما كان هناك زيادات كبيرة في متوسط عدد الكريات البيضاء، وخلايا MID، وفي عدد الخلايا الحبيبية و في ESR في مجموعة الثلث الثالث من الحمل مقارنة مع المجموعة الضابطة (P = 0.002 عدد كريات الخلايا البيضاء P = 0.030 لخلايا MID، P = 0.001 الخلايا الحبيبية و P = 0.001 لESR). وبالمثل كان هناك زيادة كبيرة في MCV في مجموعة الثلث الثالث مقارنة مع الثلث الاول (P = 0.006). يظهر ال MCHC زيادات كبيرة في الأشهر الثلاثة الاولى مقارنة بالمجموعة الضابطة ومن ثم تم تسجيل انخفاض كبير عند مجموعات الثلث الثاني والثالث مقارنة مع مجموعة الثلث الاول (P = 0.001). أظهر اختبار معامل ارتباط بيرسون علاقة طردية كبيرة بين الفيبرينوجين والخلايا البيضاء (r = ٠.١٩٦، P = 0.045)، والخلايا الحبيبية (r = ٠.٢١٩، P = 0.025) وESR (r = ٠.٢٦٠، P = 0.007) عند النساء الحوامل.

الخلاصة: تغيرت مؤشرات وقف نزيف الدم أثناء الحمل. وكانت هناك زيادة كبيرة في الفيبرينوجين، والخلايا البيضاء، MID، والخلايا الحبيبية، MCV ومعدل الترسيب خلال فترة الحمل. في المقابل اظهر كل من PT، INR، والخلايا الليمفاوية، والخلايا الحمراء، والهيموجلوبين، Hct، وMCHC، والصفائح الدموية والكالسيوم والفيبرينوجين علاقات إيجابية كبيرة مع الخلايا البيضاء، والخلايا الحبيبية وESR.

Dedication

I would like first and most to thank ALLAH for the blessing and power that made my project a reality,

I would like to extend my deepest gratitude to:

Prof. Maged M. Yassin for his valuable guidance and advice.

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APTT	Activated Partial Thromboplastin Time.
Ca	Calcium ion
ESR	Erythrocyte Sedimentation Rate
fl	Femitoliter
Hb	Hemoglobin content
Hct	Hematocrit value
INR	International Normalized Ratio
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
MCV	Mean Cell Volume
MID	Means Mid-Range absolute count
Pg	Picogram
PT	Prothrombin Time
PLT	Platelets count
RBC	Red Blood Cell
WBC	White Blood Cell

Chapter 1

Introduction

Chapter 1
Introduction

1.1 Overview

Pregnancy, also known as gravidity or gestation, is the time during which one or more offspring develops inside a woman's womb (National Institutes of Health, 2013). In a pregnancy, there can be multiple gestations, as in the case of twins or triplets. Childbirth usually occurs approximately 38 weeks after conception. In case of women who have a menstrual cycle length of 4 weeks, this is approximately 40 weeks from the last normal menstrual period (Boundless, 2015). The World Health Organization defines normal term for delivery as between 37 and 42 weeks (WHO, 2006).

Pregnancy is associated with profound anatomical, physiological, biochemical, and endocrine changes that affect multiple organs and systems (Costantine, 2014). These changes are essential to help the woman adapt to the pregnancy state and to aid fetal growth and survival. Pregnancy is typically divided into three periods, or trimesters, each of about three months (Live science.com, 2016).

The most significant hematological changes are physiologic anemia, neutrophilia, thrombocytopenia, increased procoagulant factors, and diminished fibrinolysis (Paidas et al., 2011). The changes in many aspects of hemostasis in normal pregnant women is to maintain placental function during pregnancy and to prevent excessive bleeding in delivery. Most changes in blood coagulation and fibrinolysis create a state of hypercoagulability (Prisco et al., 2005). As most coagulation factors increase in normal pregnancy, the prothrombin time (PT) and activated partial thromboplastin time (APTT) may be shortened (Erhabor et al., 2013; Haram et al., 2009). Fibrinogen level is increased during normal pregnancy. The hemostatic changes noted during pregnancy, normalize after delivery with 4-6 weeks (Hellgren, 2003).

According to World Health Organization, one woman dies every minute from a pregnancy-related complication. The main causes of mortality are antepartum and postpartum hemorrhage, unsafe abortion, eclampsia, obstructed labor and infection (Chandra et al., 2012).Thus, it is important to know variations in hemostatic and hematological profiles during pregnancy as well as delivery such that adverse incidents leading to minimized maternal mortality. No previous study investigated hemostatic parameters in normal pregnant women in Gaza strip. The routine tests is limited to measurement of PT, APTT and fibrinogen values usually after the occurrence of hematological complications. Therefore, this will be the first study to assess hemostatic and hematological profile during the three trimesters of pregnancy in pregnant women from Gaza strip.

1.2 General objective

The general objective of the present study is to assess hemostatic parameters of normal pregnant women in Gaza strip.

1.3 Specific objectives

1. To determine PT, INR, APTT, and fibrinogen level in normal pregnant women compared to non pregnant controls.

2. To evaluate leukocytes and platelets in normal pregnant and non pregnant women.

3. To estimate primary and secondary blood indices and erythrocyte sedimentation rate (ESR) in normal pregnant and non-pregnant women.

4. To determine Ca level in normal pregnant women with respect to non pregnant women.

5. To verify the possible relationship between fibrinogen and the other studied parameters of the study population.

1.4 Significance

The mortality rate of mother and fetus is increased as a result of hemostatic and hematological complications in Gaza strip. Thus, it is important to do PT, INR, APTT and fibrinogen to every pregnant women as a routine test to monitoring pregnancy to predict and/ or to improve pregnancy outcome dependent on the hemostatic and hematological parameters. In addition, there is lack of research on hemostatic changes during pregnancy in Gaza strip.

Chapter 2

Literature Review

Chapter 2
Literature Review

2.1 Definition of pregnancy

Pregnancy is a period of reproduction during which a women carries one or more live offspring from implantation of a fertilized zygote in the uterus throughout gestation. Childbirth usually occurs about 38 weeks after conception; in women who have a menstrual cycle length of four weeks, this is approximately 40 weeks from the start of the last normal menstrual period (WHO, 2006). One scientific term for the state of pregnancy is gravidity (adjective " gravid "), Latin for " heavy " and a pregnant female is sometimes referred to as a gravida. Similarly, the term parity (abbreviated as "para") is used for the number of previous successful live births. Medically, a women who has never been pregnant is referred to as a "nulligravida", a woman who is (or has been only) pregnant for the first time as a "primigravida", and a women in subsequent pregnancies as a multigravida or "multiparous" (Medical Dictionary/The Free Dictionary, 2015).

2.2 Initiation of pregnancy

About once every 28 days, in the middle of a woman's menstrual, an ovum bursts from one of her ovaries, and is drawn into one of two fallopian tubes that lead to the hollow uterus. While the ovum is traveling, the spot on the ovary from which it was released, now called the corpus luteum, secretes hormones that prepare the lining of the uterus to receive a fertilized ovum. If pregnancy does not occur, the corpus luteum shrinks, and the lining of the uterus is discarded two weeks later with menstruation (Berk, 2011).

After sexual intercourse, sperms are transported upward from the vagina and through the uterus and fallopian tube, where fertilization usually takes place. One spermatozoon out of hundreds of millions ejaculated by the man may penetrate the outside layer of the ovum and fertilize it. Through fertilization, the egg is activated to begin its developmental process, and the haploid nuclei of the two gametes come together to form the genome of a new diploid organism. The fertilized egg, known as

a zygote, then moves toward the uterus, a journey that can take up to a week to complete. Cell division begins approximately 24 to 36 hours after the male and female cell unite. Cell division continues at a rapid rate and the cells then develop into what is known as a blastocyst, which arrives at the uterus and attaches to the uterine wall, a process known as implantation. The mass of cells is now known as an embryo (Guyton and Hall, 2011).

2.3 Duration of pregnancy

Healthcare professionals name three different dates as the start of pregnancy:

- The first day of the woman's last normal menstrual period,
- The date of conception (about two weeks before her next expected menstrual period), and
- The date of implantation (about one week after conception).

The most common system used among healthcare professionals is Naegele's rule which calculates the expected due date from the first day of the last normal menstrual period (LNMP) regardless of factors known to make this inaccurate, such as a shorter or longer menstrual cycle length. Pregnancy most commonly lasts for 40 weeks according to this LNMP-based method, assuming that the woman has a predictable menstrual cycle length of close to 28 days and conceives on the 14^{th} day of that cycle, and a birth between 37 and 42 weeks LNMP is considered full-term (Norwitz, 2007).

There is a standard deviation of 8-9 days surrounding due dates calculated with even the most accurate methods. This means that fewer than 5% of births occur at exactly 40 weeks; 50% of births are within a week of this duration, and about 80% are within 2 weeks (Kieler et al., 1995). Pregnancy is considered "at term" when gestation attains 37 complete weeks but is less than 42 weeks. Events before completion of 37 weeks are considered preterm; from week 42 events are considered post term (Rand et al., 2000). When a pregnancy lasts less than 37 weeks or exceeds 42 weeks, the risk of complications for both the woman and the fetus increases significantly (American College of obstetricians and Gynecologists, 2006; Norwitz, 2007).

2.4 Trimesters of pregnancy

As soon as a woman becomes pregnant, her body begins to change so that she can support both herself and the unborn baby. Pregnancy has three trimesters, each of which is marked by specific fetal developments.

2.4.1 First trimester

Traditionally, medical professionals have measured pregnancy from a number of convenient points, including the day of last menstruation, ovulation, fertilization, implantation and chemical detection. In medicine, pregnancy is often defined as beginning when the developing embryo becomes implanted in the endometrial lining of a woman's uterus. The first 12 weeks of pregnancy are considered to make up the first trimester (Curtis and Schuler, 2011).

During the first trimester, the maternal body undergoes many changes. Hormonal changes affect almost every organ system in the body. These changes can trigger symptoms even in the very first weeks of pregnancy (MedicineNet.com, 2016):

- Tiredness
- Swollen breasts and the nipples and areolas begin to darken.
- Upset stomach with or without throwing up (morning sickness).
- Cravings or distaste for certain foods.
- Mood swings.
- Constipation (trouble having bowel movements).
- Frequent urination.
- Headache.
- Weight gain or loss.

Fetal development during the first trimester begins with multiplying of zygote and forming of a blastocyst in the first week. During the second week, the blastocyst burrows into the uterine lining. Structures that feed and protect the developing organism begin to form amnion, chorion, yolk sac, placenta, and umbilical cord. In the third and four weeks, primitive brain and spinal cord appear. Heart, muscles, ribs, backbone, and digestive tract begin to develop and the embryo becomes 6 mm in length. During 5-8 weeks, many external body structures (face, arms, legs, toes, fingers) and internal organs form. The sense of touch begins to develop, and the

embryo can move where it becomes 2.5 cm in length. During 9-12 weeks, rapid increase in size begins. Nervous system, organs, and muscles become organized and connected, and new behavioral capacities (kicking, thumb sucking, mouth opening, and rehearsal of breathing) appear. External genitals are well formed, and the fetus's sex is evident. The embryo becomes 7.5 cm in length (Berk, 2011; American Pregnancy Association, 2015).

2.4.2 Second trimester

Weeks 13 to 28 of the pregnancy are the second trimester. It is often called the "golden period" because many of the unpleasant effects of early pregnancy such as nausea and fatigue disappear. The abdomen will expand as the baby continues to grow. And before this trimester is over, mother will feel her baby beginning to move. The women during the second trimester may have (Womenshealth.gov, 2016):

- Body aches, such as back, abdomen, groin, or thigh pain.
- Stretch marks on abdomen, breasts, thighs, or buttocks.
- Darkening of the skin around nipples.
- A line on the skin running from belly button to pubic hairline.
- Patches of darker skin, usually over the cheeks, forehead, nose, or upper lip (mask of pregnancy).
- Numb or tingling hands (carpal tunnel syndrome).
- Itching on the abdomen, palms, and soles of the feet.
- Mild swelling of the ankles, fingers, and face.

During the second trimester, the fetus continues to enlarge rapidly. In the middle of this period, fetal movements can be felt by the mother. Vernix and lanugo keep the fetus's skin from chapping in the amniotic fluid. Most of the brain's neurons are present by 24 weeks. Eyes are sensitive to light, and the fetus reacts to sound. The placenta fully functions and the fetus makes insulin and urinates. At the end of the second trimester, the fetus becomes 30 cm in length and 820 gm in weight (Berk, 2011).

2.4.3 Third trimester

Weeks 29 to 40 of the pregnancy are the third trimester. In this period, final weight gain takes place, which is the most weight gain throughout the pregnancy. The fetus grows rapidly and his or her movements become stronger and more frequent. Some new maternal body changes might notice in the third trimester include (Mayo clinic, 2016):

- Shortness of breath
- Heartburn.
- Swelling of the ankles, fingers, and face.
- Hemorrhoids.
- Tender breasts, which may lead a watery pre-milk called colostrum.
- Belly button may stick out.
- Trouble sleeping.
- The baby "dropping " or moving lower in the abdomen.
- Contractions, which can be a sign of real or false labor.

The fetus has a good chance of survival if born during this time. Size increases, lungs mature, rapid brain development causes sensory and behavioral capacities to expand. In the middle of this period, a layer of fat is added under the skin. Antibodies are transmitted from mother to the fetus protect against disease. Finally, fetus becomes 50 cm in length and 3.4 kg in weight. Most fetuses rotate into an upside-down position in preparation for birth (Berk, 2011).

2.5 Hemostatic and hematological profiles during pregnancy

Hemostasis is a complex interaction between the vessel wall and components of blood, which prevents excessive blood loss after vascular damage while maintaining a viable circulation by preventing thromboembolic conditions (Nordenhem, 2006). It is regulated by vascular wall, platelets and coagulation cascade by a set of processes to maintain blood in a fluid, clot-free state and to induce a rapid and localized hemostatic plug at the site of vascular injury (Kumar et al., 2005 and Riddel et al., 2007).

Pregnancy is accompanied by major changes in the coagulation and fibrinolytic system. There are marked increases in fibrinogen and factor VIII level. These changes to minimizing the hazard of hemorrhage during and after placental separation (Durotoye et al., 2012). Therefore, pregnancy is recognized as a hypercoagulable state that protect women from potentially hemorrhage during placentation and the post-partum period (Hellgren, 2003). Normal pregnancy has been associated with alteration of the hemostatic system, which has been linked to increased risk of thromboembolic complication and venous thromboembolism (VTE) in pregnancy and post-partum period with VTE occurring in 0.7/1000 women. It is about 3-4x higher in the puerperium than in non-pregnant women. (McColl et al., 1997; Eichinger, 2005; Retzinger, 2010).

The coagulation cascade is an activated state with about 20-200% increase in fibrinogen and factors II, VII, VIII, X, and XII while the level of factor XI and XIII decrease (Johnson, 1997; Hellgren, 2003). Fibrinogen level increases from about 300mg/dl pre-pregnancy to as much as 600mg/dl at term, averaging about 450mg/dl (Baker et al., 1999). Estrogen and progesterone are an important hormones which are necessary for maintenance of pregnancy, these hormones increase several folds and these especially estrogen stimulate hepatocyte thereby increasing the production of virtually all coagulation factors (Notelowitz et al., 1982). Persistent hypercoagulation has been demonstrated during the first 3 weeks of delivery; however, pregnancy related hypercoagulable state should resolve by 6-8 weeks post-partum (Saha et al., 2009).

In pregnancy, there is a gradual increase in circulating blood volume of up to 1.5 L by the third trimester (Tran, 2005). Although red cell mass increase, a physiologic anemia occurs in pregnancy as there is an even greater increase in plasma volume. In addition, Lurie and Mamet (2000) found that erythropoietin and erythrocyte production are increased during normal pregnancy while erythrocyte mass per unit of body weight remains constant throughout the entire pregnancy, and hemoglobin and hematocrit continuously decrease into the third trimester. Erythrocyte life span is decreased during normal pregnancy due to emergency hemopoiesis in response to

elevated erythropoietin levels. The two most common causes of anemia in pregnancy are iron deficiency and acute blood loss (American College of Obstetrician and Gynecologists, 2008).

Thrombocytopenia is the second most common hematological finding in pregnancy after anemia. It affects 7-10 % of all pregnant women. The cause for the physiologic decrease in platelet count is multifactorial and is related to hemodilution, and increased platelet consumption and increased platelets aggregation by increased levels of Thromboxane A2. (Bockenstedt, 2011, Khellaf et al., 2012; Perepu, 2013). Gestational thrombocytopenia occurs in more than 70% of cases with thrombocytopenia in pregnancy. Although the pathophysiology of gestational thrombocytopenia is unknown, it is thought to be related to increase activation and peripheral consumption. Gestational thrombocytopenia is occurring in the latter half of pregnancy, from the mid-second to third trimester and women are typically asymptomatic. Gestational thrombocytopenia is self-limiting and resolve within 1 to 2 months after delivery. It is not associated with adverse outcomes for the baby (Perepu, 2013).

Leukocytosis is another hematological feature during pregnancy. Leukocytosis is due to increased inflammatory response during normal pregnancy, which can be as a consequence of selective immune tolerance, immunosuppression and immunomodulation of fetus (Osonuge et al., 2011). Tzur et al. (2013) has shown that leukocytosis during first trimester is associated with complication during pregnancy.

Osoagbaka et al. (2000) determined changes of some hematological parameters in 270 pregnant and 40 clinically healthy non-pregnant Nigerian women. There was a decrease in mean hemoglobin of pregnant women during the trimester (11.20±1.88; 10.72±2.84; 10.47±2.24 g/dl). There was also decrease in packed cell volume, PCV (32.54±4.86; 30.30±9.64; 30.30±6.80%). The corresponding figures for non-pregnant women were 12.54±1.90 g/dl and 35.35±2.00%, respectively. The erythrocyte sedimentation rate in the pregnant group showed significant increased from the first to the third trimesters with a statistical significance at 5% (P= 0.005)

and 1% (P= 0.001) confidence levels. The WBC total counts showed moderate increase from the first trimester with an increase in neutrophil count as the pregnancy advanced.

Laboratory tests of maternal hematological parameters in 211 full term pregnant women showed a low mean level of hemoglobin (Papadopol et al., 2001). Similarly, Tran (2005) pointed out that in pregnancy, there is a gradual increase in circulating blood volume of up to 1.5 L by the third trimester. As there is a smaller increase in red cell mass, there is a decrease in hematocrit and hemoglobin concentrations.

Hellgren, (2003) studied hemostasis during normal pregnancy, in her study most blood coagulation factors and fibrinogen levels increase during pregnancy, slightly decreased in APTT, increased PT measured as international normalized ratio (INR) of less than 0.9 have been reported as well. Platelet count within normal range expect during the third trimester (gestational thrombocytopenia), 80 to 150 $x10^9$ /L. The bleeding time is unchanged during normal pregnancy. The hemostatic changes, noted during pregnancy, normalize after delivery within 4 to 6 weeks.

Uchikova et al. (2005) studied the changes in the hemostatic variables in 35 normal pregnant Bulgarian women and compare them with 35 healthy non-pregnant women. The result showed significant higher values for prothrombin time (PT), fibrinogen, thrombin time (TT), activity of factor VII and factor X ($P<0.0001$) in pregnant women. In addition, no significant values were found for APTT.

Asif et al. (2007) found that hemoglobin decreased with increasing gestational age in 150 pregnant Pakistani women. In addition, James et al. (2008) evaluated hemoglobin concentration, PCV, MCV, MCH; MCHC, WBC, RBC and platelet counts in 157 healthy pregnant Jamaican women. The results showed changes by trimester in all measured variables. For most of the indices, the changes achieved levels of significance across trimesters. These changes were however in keeping with the expected physiological response in pregnancy and the values were similar to the published international norms.

Osonuge et al. (2011) evaluated the values of some major hematological parameters in 33 healthy pregnant women (11 in first trimester, 11 in second trimester and 11 in third trimester) aged 20-40 years as the study group. Eleven non-pregnant age-matched women were used as controls. The study group exhibited statically significant lower values of PCV, monocyte and lymphocyte while WBC, eosinophil and ESR were significantly increase compared to controls. However, there was no significant difference in all hematological parameters among the three trimesters.

Chandra et al. (2012) reported leukocytosis, neutrophilia, lymphocytopenia and thrombocytopenia during pregnancy. Fibrinogen and clotting factors VII, VIII, X, XII and vWF were increased remarkably as gestation progress. Increased levels of coagulation factors due to increased protein synthesis mediated by the rising estrogen levels. APTT is usually shortened, by up to 4 seconds in the third trimester, largely due to the hormonally influenced increase in factor VIII. However, no marked changes in PT.

In Nigerian pregnant women, Durotoye et al. (2012) in his study found that PT and fibrinogen concentration were significantly affected by the gestational age of the pregnancy with mean PT of 13.2±1.9 seconds, 12.7±1.5 seconds, and 12.1±1.5 seconds and fibrinogen concentration of 4.1±1.5 g/l, 5.1±1.7 g/l and 5.2±1.3 g/l in 1^{st}, 2^{nd} and 3^{rd} trimesters respectively, P values 0.001 and 0.001. However, gestational age of the pregnancy had no significant effect on APTT and platelets count (p values 0.405 and 0.880, respectively).

Das et al. (2013) determined the effect of pregnancy on hematological parameters in 30 healthy pregnant women and 10 non-pregnant women as controls. The result showed significant lower values in hemoglobin, PCV, monocyte and lymphocyte while WBC, eosinophil and ESR were significantly elevated among the three trimesters.

Verma et al. (2013) studied the hematological parameters in 100 pregnant females in advanced pregnancy (of gestational age 32-40 weeks) and compared them with 25

non pregnant women which were have the same range of age as pregnant females. The result were progressive fall in Hb level, RBC count, and hematocrit from the end of the first trimester until a few weeks before term returning to normal 1-2 months post-partum, and gradually increase in ESR.

Ichipi-Ifukor et al. (2013) investigated the variation in some hematological indices during 200 normal pregnant Nigerian women and compared them with 80 non-pregnant women. In his study, there was significant decrease in PCV of the test group was (32.58±4.01%) when compared to control (37.07±3.19%). Similarly, the result of hemoglobin showed a significant difference between the test (10.00±1.23 g/dl) and the control group (11.71±1.32 g/dl) while granulocytes and platelets also showed significant decrease and lymphocytes significantly increase; the total white blood cell count (WBC) showed no significant differences; there was an increased level comparing to the control.

Ifeanyi et al. (2014) observed significant changes in mean values of RBC, Hct, MCV, MCH, WBC, lymphocyte, monocyte, and eosinophils of 40 normal pregnant Nigerian women when compared to 40 non-pregnant women ($P<0.05$).

Purohit et al. (2015) studied the hematological profile of normal pregnant women in Western India. The study group consisted of 302 healthy pregnant women and 94 non pregnant women matched with age and sociodemographic state. They recorded variations in platelet count and WBC during pregnancy, while other parameters like RBC count, blood indices, and hemoglobin concentration remain unaltered during pregnancy.

Imoru and Buseri, (2015) showed significantly lower value of platelets count and higher value of factor VIII activity of ($248.2 \pm 78.8 \times 10^9$ /l and 110±46 % in pregnant women compared to $289.4 \pm 68.7 \times 10^9$ /l and 96.8±38.2 % respectively, in non-pregnant women. While values of PT, INR and APTT in pregnant and non-pregnant showed no significant differences ($p> 0.05$).

Mohamed et al. (2015) studied physiological changes in some hematological and coagulation profile among Sudanese healthy pregnant women. The results were presented as follow: mean value of WBC was 7.580 cell/$mm^{3,}$ RBCs were 4.1×10^{12} /L, Hb was 11.79 g/dl, platelets were 256×10^{9} /L, PT mean value of the study group was 13.40 seconds and APTT was 36.20 seconds. There were no significant differences in PT, APTT, platelets, Hb and RBCs among the pregnant women in the three trimesters except WBCs, which showed significant differences among three trimesters of pregnancy.

Chapter 3

Materials and Methods

Chapter 3
Materials and Methods

3.1 Study design

The study is a case control design. Case - control studies are often used to identify factors that may contribute to a medical condition by comparing subjects who have that condition/disease (the "cases") with patients who do not have the condition/disease but are otherwise similar (the "controls"). Case-control studies are quick, widely used, relatively inexpensive to implement, require comparatively fewer subjects, and allow for multiple exposures or risk factors to be assessed for one outcome (Mann, 2003; Song and Chung, 2010).

3.2 Study population

The study population comprised 140 women aged 18-40 years; 105 apparently healthy pregnant women and 35 healthy non-pregnant with matched age as controls.

3.3 Sample size and sampling

A total 105 pregnant women were selected from Palestinian Family Planning and Protection Association between September 2015 and December 2015. They sub-divided into three groups each consist of 35 women distributed into 1^{st}, 2^{nd} and 3^{rd} trimesters of pregnancy, respectively. A total of 35 healthy non-pregnant women were selected from general population and served as controls. Pregnant and non-pregnant women were aged matched.

3.4 Selection criteria

3.4.1 Inclusion criteria

Healthy non-pregnant and pregnant women from Gaza strip aged 18-40 years.

3.4.2 Exclusion criteria

- Pregnant women who treated with anticoagulant therapy as aspirin, heparin, etc.
- Women over age 40 years because pregnancy in this age is considered to be high risk.

3.5 Ethical consideration

The necessary approval to conduct the study was obtained from Helsinki committee in Gaza strip. Consent form obtained from all participant to ensure their voluntary participation (appendix 1).

3.6 Data collection

3.6.1 Questionnaire interview

A meeting interview was used for filling in a questionnaire, which designated for matching the study need (appendix 2). All interviews were carried out face to face by the researcher herself. During the survey, the interviewer explained any of the questions that were not clear. The questionnaire was based on Palestinian Family Planning and Protection Association questionnaire and on other international studies with some modifications (Palestinian Family Planning and Protection Association, 2015; Women Health Specialists, 2015). Most questions were one of two types: the yes/no question, which offers a dichotomous choice; and the multiple choice question, which offers several fixed alternatives (Backestrom and Hursh-Cesar, 2012).

The questionnaire was validated by five experts in the fields of obstetrics and gynecology, public health, physiology and nutrition. The questionnaire included questions on sociodemographic data (age, education, employment and family income/month), medical history (previous pregnancy, pregnancy outcome, problems in previous pregnancy), clinical data (problems during this pregnancy, medication), and food and drink intake of the study population.

3.6.2 Specimen collection and hematological analysis

Blood sample were collected from 105 pregnant women (35 in the first trimester, 35 in the second trimester and 35 in the third trimester) as well as from 35 healthy non-pregnant control women. About 6 ml venous blood samples were drawn by the researcher herself from pregnant and non-pregnant women. Each blood sample was divided into EDTA tube (2ml), 3.2% Tri-Sodium Citrate tube (1.8 ml) and plain tube (2ml). EDTA tube was used for complete blood count, then added blood sample to citrated tube for ESR analysis. The CBC and ESR analysis should be done at the same day of blood collection. Tri sodium citrate tube was used for PT, INR, APTT

and fibrinogen analysis. Plasma samples were obtained by centrifugation at room temperature at 4000 rpm for 10 minutes to analyzed samples during 3 hours after blood collection. Plain tubes were left for short time to allow blood to clot. Then, serum samples were obtained by centrifugation at room temperature at 4000rpm for 5 minutes to measure Ca concentration.

3.7 Hemostatic analysis

3.7.1 Determination of PT and INR

BioMed- Liquiplastin for PT determination. By using Biomed Diagnostics reagent.

Lot number: LQ302528.

- **Principle**

  Tissue Thromboplastin in the presence of calcium activates the extrinsic pathway of human blood coagulation mechanism. When BioMed-LIQUIPLASTIN reagent is added to normal citrated plasma, the clotting mechanism is initiated, forming a solid gel clot within a specific period of time. The time required for clot formation would be prolonged if there is acquired or congenital deficiency of factors/ factor activity in the extrinsic pathway of the coagulation mechanism or reduction in the activity of Vitamin K dependent clotting factors during oral anticoagulant therapy.

- **Reagent:**

  LIQUIPLASTIN is liquid calcified liquiplastin reagent ready to use.

- **Procedures:**

  1. Bring the reagent vial to room temperature and mixed the contents gently.
  2. Aspirate from the reagent vial enough reagents for immediate testing requirements in clean and dry plastic tube and pre warmed in water bath at 37 C^{o} for 5-10 minutes.
  3. 100 μl of plasma was pipetted into clean and dry plastic tube and pre- warmed for 3-5 minutes in water bath at 37 C^{o}
  4. 200 μl of pre warmed BioMed -LIQUIPLASTIN reagent was added to plasma tube and start a stopwatch.

5. Shake the tube gently to mix contents and stop the stopwatch as soon as the first fibrin strand is visible and the clot formation begins record the time in seconds.
6. Repeat the steps from 3 to 5 for a duplicate test on the same sample.
7. Find the average of the duplicate test values. This is PT.

- **Calculation:**

  The results may be reported directly in terms of the mean of the double determination of PT of the test plasma in seconds.

  Or as ratio "R": R= mean of the patient plasma PT in seconds/ MNPT for the reagent.

  Or as International Normalized Ratio (INR), INR= (R^{ISI} ,where ISI= International Sensitivity Index of the reagent.

  It recommended by the WHO that MNPT should be established for each lot of PT reagents by each laboratory, since PT result are dependent on the combination of reagent lot, instrument and technique followed at each laboratory.

  Usually plasma from at least 20 normal healthy individuals should be used to establish the MNPT. The average of such PT results in seconds= MNPT.

- **Normal value**

  The expected range is between 10 and 15 s.

- **References:**

Biggs R. and R. G. McFarlane: Human blood coagulation and its disorders, Blackwell scientific publications, Oxford, 1962.

3.7.2 Determination of activated partial thromboplastin time (APTT)

For quantitative determination of APTT the Speedlab-LIQUICELIN- E activity in plasma. By using SPEEDLAB Biochemistry Solutions. LOT number: 303522.

- **Principle**

Cephaloplastin activates the coagulation factors of the intrinsic pathway of the coagulation mechanism in the presence of calcium ions. APTT is prolonged by deficiency of one or more of these clotting factors of the intrinsic pathway and in the presence of coagulation inhibitors like heparin.

- **Reagent**

Speedlab-LIQUICELIN- E

Calcium chloride

- **Procedures**

1. 100 µl plasma was pipetted into dry and clean plastic tube.
2. Plasma was pre-warmed in water bath for 1-2 minutes at 37C°.
3. 100 µl APTT reagent was added to plasma and incubated for 3 minutes at 37C°.
4. Added 100 µl pre warmed calcium chloride and start stop watch.
5. Shake the tube gently to mix contents and stop the stopwatch as soon as the first fibrin strand is visible and the clot formation begins record the time in seconds.

- **Normal value**

The expected range is between 30 and 35 s.

- **References:**

Biggs R. and R. G. McFarlane: Human blood coagulation and its disorders, Blackwell scientific publications, Oxford, 1962.

3.7.3 Determination of fibrinogen concentration

Fibrinogen Clauss method for determination of fibrinogen. LABKIT reagent. LOT number: 332.

- **Test summary**

Fibrinogen in presence of an excess of thrombin concentration changes into Fibrin.

The time for clot formation in dilute plasma is inversely proportional to the fibrinogen concentration in the sample.

- **Reagents composition**

R1	Bovine thrombin
R2	Imidazole buffer
R3	Caolin solution

- **Reagent preparation**

R1: dissolved the contents with 2.0 ml of distilled water and mixed gently to dissolve contents. Stability: 7 days at 2-8°C or for 1 month at -20°C.

R2: mixed before used.

R3: ready for use reagent.

Calibrator: dissolved the contents with 1.0 ml of distilled water and mixed gently. Stability: 8 hours at 2-8°C.

- **Test procedure**

1. Diluted the citrated plasma and control 1/10 with Imidazole buffer:
   50 µl plasma + 450 µl Imidazole buffer.
   The diluted sample must be processed in 1 hour.
2. Prepare the following dilutions of the calibrator in Imidazole buffer.

Calibrator dilution	1/40	1/30	1/20	1/10	1/5
Imidazole buffer (mL) Calibrator (mL)	3.9 0.1	2.9 0.1	1.9 0.1	0.9 0.1	0.4 0.1
Factor	10/40*	10/30*	10/20*	10/10*	10/5*
Concentration (mg/dl)	0.25*×c	0.33*×c	0.5*×c	1*×c	2*×c

3. Add 20 µl of R3 to 0.2 ml of each dilution, and allow to reach 37°C for 4–6 minutes.
4. Add 0.1 ml of R1 and time clot formation. Do not pre-warm thrombin R1.

- **Calculation**

1. Calculate the mean of duplicated clotting times immediately after reaction. Use all five of calibrator points to construct a log-log curve that plots fibrinogen concentration (mg/dl) vs. clotting time (s).
2. Draw the straight line of best fit. Examine the curve and, if necessary, omit non-linear points. The final curve must consist of at least three consecutive points. Constructing the curve with only

the most linear points will produce the best recovery on control and patient samples.

3. The following curve is only orientative. It will change with lot and concentration of the calibrator, as well as, with the instrument used.

Time (s)	Concentration (mg/dl)
18.1	608
26.4	304
49.6	152
84.7	76
153	38

4. Find the clotting time of quality control and patient samples on the curve and read the corresponding fibrinogen value.

5. If clotting times for the 1/10 dilution fall outside the linear curve, prepare 1/5 or 1/20 dilutions as needed. If the sample is diluted 1/5, divide the result from the standard curve by 2; if the sample was diluted 1/20, multiply the curve result by 2 to get the final result.

- **Normal value**

The expected range 200-400 mg/dl.

- **References:**

Young DS. Effects of disease on clinical lab. Tests, 4th ed AACC 2001.

3.8 Hematological analysis

3.8.1 CBC: Cell Blood Count

Blood samples were processed by an automatic counter for hemoglobin concentration and other whole blood component concentrations by using Mindray BS 3000 (China).

3.8.2 ESR: Erythrocyte Sedimentation Rate

Whole blood was mixed with sodium citrate and then added to a standardized calibrated tube, which was allowed to sit for 60 min. After 60 min, sedimentation was measured by recording the number of millimeters between the top of the sedimented red blood cells and the zero mark at the top of the tube.

- **Normal value**

  The expected range 0-15 mml/ 1hour

3.9 Determination of calcium

Serum calcium was determined by Photometric test with cresolphthalein complexone (Thomas, 1998) using DiaSys reagent kit.

- **Principle:**

Cresolphthalein complexone reacts with calcium ions in alkaline medium forming a red-violet color. Interference by magnesium is eliminated by addition of 8-hydroxy-quinoline

- **Reagents:**

Reagent	Components	Concentrations
Reagent 1	Ethanolamine Detergent pH 10.7	600 mmol/L
Reagent 2	2-Cresolphthalein complexone 8-Hydroxyquinoline Hydrochloric acid pH 1.1	0.06 mmol/L 7 mmol/L 20 mmol/L
Reagent 3	Standard:	10 mg/dL

- **Preparation and stability of working reagent:**

Four parts of R1 were mixed with 1 part of R2

Stability: 3 days at 2-8 ^{o}C

- **Procedure:**

Wavelength 570 nm, Hg 578 nm (550-590 nm)

Temperature 37°C

Cuvette 1 cm light path

Reading against reagent blank was done

	Blank	Standard	Sample
Working reagent	1 ml	1 ml	1 ml
Distilled water	20 µl	-	-
Standard	-	20 µl	-
Sample	-	-	20 µl

Mixing and reading the optical density (OD) after a 5 minute incubation was done. The final color is stable for at least 15 minutes.

- **Calculation:**

$$\frac{\text{OD Sample}}{\text{OD Standard}} \times n = \text{sample calcium concentration (mg/dl)}$$

n = standard calcium concentration

- **Normal value**

The expected range 8.4-10.3 mg/dl.

3.10 Statistical analysis

Data were computer analyzed using SPSS/PC (Statistical Package for the Social Science Inc. Chicago, lllinois USA, version 21.0) statistical pachage.

- Simple distribution of the study variables and the cross tabulation were applied.
- Chi-square (χ^2) was used to identify the significance of the relations, associations, and interactions among various variables. Yates's continuity test, $\chi^2_{(corrected)}$, was used when not more than 20% of the cells had an expected frequency of less than five and when the expected numbers were small.
- Analysis of variance (ANOVA) was applied.
- Range as minimum and maximum values was used.
- Analysis of Scheffe test was applied.
- Pearson's correlation test was used.
- The results in all the above-mentioned procedures were accepted as statistical significant when the p-value was less than 5% ($p<0.05$).
- Fibrinogen histogram was plotted using Excel program version 11.
- Correlation graphs were plotted using SPSS/PC version 21.

Chapter 4

Results

Chapter 4
Results

4.1 Socio-demographic data of the study population

The present study is a case control design. The study population comprised 105 normal pregnant woman (sub-divided into three groups each contains 35 women distributed into 1st, 2nd and 3rd trimester of pregnancy) and 35 healthy non-pregnant women (control group). Table 4.1 summarizes the sociodemographic data of the study population. Age classification showed that 3 (8.6%) controls, and 4 (11.4%) pregnant women in the 1st, 2nd and 3rd trimesters each were ≤20 years old. Age group 21-30 years comprised 17 (48.6%) controls, and 17 (48.6%), 16 (45.7%), and 16 (45.7%) pregnant women in the 1st, 2nd, and 3rd trimesters, respectively. Controls and pregnant women aged >30 years old were 15 (42.9%), 14 (40.0%), 15 (42.9%) and 15 (42.9%), respectively. The difference between pregnant and non-pregnant women in term of age distribution was non-significant ($\chi^2_{(corrected)}$=0.084, P=0.998). The mean ages of controls and pregnant women were 29.0±5.1, 28.6±6.2, 28.7±5.8 and 28.9±6.1 years old, respectively. There was no significant differences between mean ages of pregnant and non-pregnant women (F=0.414, P=0.743). Analysis of the educational status of the study population showed no significant differences at various educational levels between pregnant and non-pregnant women ($\chi^2_{(corrected)}$=3.368, P=0.761). Regarding employment, 17 (48.6%) controls, and 7 (20.0%), 8 (22.9%) and 3 (8.6%) pregnant women were employed whereas 18 (51.4%) controls, and 28 (80.0%), 27 (77.1%) and 32 (91.4%) were unemployed. The difference between various groups was significant with higher number of unemployed pregnant women ($\chi^2_{(corrected)}$=13.600, P=0.004). Similarly, there was significant difference between pregnant women in term of family income per month with lower income among pregnant women ($\chi^2_{(corrected)}$=20.950, P=0.002).

Table (4.1): Sociodemographic data of the study population

Socio-demographic	Non Pregnant Control (n=35) No. (%)	Pregnant Woman Trimesters			χ^2	P-value*
		First (n=35) No. (%)	Second (n=35) No. (%)	Third (n=35) No. (%)		
Age (years)						
≤20	3 (8.6)	4 (11.4)	4 (11.4)	4 (11.4)	0.084	0.998
21-30	17 (48.6)	17 (48.6)	16 (45.7)	16 (45.7)		
>30	15 (42.9)	14 (40.0)	15 (42.9)	15 (42.9)		
Mean±SD	29.0±5.1	28.6±6.2	28.7±5.8	28.9±6.1		
Education						
University	24 (68.6)	18 (51.4)	15 (42.9)	20 (57.1)	3.368	0.761
Secondary	10 (28.6)	14 (40.0)	17 (48.6)	13 (37.1)		
Preparatory	1 (2.6)	3 (8.6)	3 (8.6)	2 (5.7)		
Employment						
Yes	17 (48.6)	7 (20.0)	8 (22.9)	3 (8.6)	13.600	0.004
No	18 (51.4)	28 (80.0)	27 (77.1)	32 (91.4)		
Family income/month						
<1000	9 (25.7)	22 (62.9)	18 (51.4)	12 (34.3)	20.950	0.002
1000-2000	9 (25.7)	4 (11.4)	9 (25.7)	18 (51.4)		
>2000	17 (48.6)	9 (25.7)	8 (22.9)	5 (14.2)		

*P-value of χ^2 (corrected) test

P<0.05: Significant, P>0.05: Not significant

4.2 Medical history of the study population

Table 4.2 provides medical history of the study population. When asked" have you been pregnant before? Higher number of controls 34 (97.1%) said yes compared to their counterparts of pregnant women of 28 (80.0%), 29 (82.9%) and 28 (80%) in the 1st, 2nd and 3rd trimesters, respectively. However, the difference between the various groups was not significant (χ^2 *(corrected)*=3.866, P=0.276). Out of them, the number of controls who had live babies 34 (100%) was also higher than their counterparts of pregnant women in each trimester (P>0.05). In general, the occurrence of problems in the previous pregnancy was relatively low registering 7 (20.0%) in controls and 4 (11.4%), 5 (14.3%), and 4 (11.4%) in pregnant women in the 1st, 2nd, and 3rd trimesters of pregnancy, respectively (χ^2 *(corrected)*=0.700, P=0.873).

Table (4.2): Medical history of the study population

Medical history	Non Pregnant Control (n=35) No. (%)	Pregnant Woman Trimesters			χ^2	P-value
		First (n=35) No. (%)	Second (n=35) No. (%)	Third (n=35) No. (%)		
Have you been pregnant before						
Yes	34 (97.1)	28 (80.0)	29 (82.9)	28 (80.0)	3.866	0.276*
No	1 (2.9)	7 (20.0)	6 (17.1)	7 (20.0)		
Outcome of pregnancy						
Abortion	14 (41.2)	11 (39.3)	11 (37.9)	9 (32.1)	0.264	0.966
Live baby	34 (100)	26 (92.9)	28 (96.6)	26 (92.9)	0.058	0.966
Dead baby	2 (5.9)	4 (14.3)	3 (10.3)	0 (0)	1.956	0.582*
Previous pregnancy problems**						
Yes	7 (20.0)	4 (11.4)	5 (14.3)	4 (11.4)		
No	28 (80.0)	31 (88.6)	30 (85.7)	31 (88.6)	0.700	0.873*

*P-value of $\chi^2_{(corrected)}$ test

P>0.05: Not significant.

** Previous problems included anemia, vaginal bleeding, headache, and hemorrhage disorders.

4.3 Clinical data of the study population

As indicated in table 4.3, the frequency of the problems reported in pregnancy were increased with the progression of pregnancy: 3 (8.6%), 7 (20.0%), 12 (34.3%) in the 1st, 2nd and 3rd trimesters, respectively. However, the difference between the three trimesters was not significant (χ^2=5.535, P=0.063). Medication also showed non-significant difference between pregnant women who received medication compared to pregnant women who did not ($\chi^2_{(corrected)}$=0.198, P=0.906).

Table (4.3): Clinical data of the study population

Clinical Data	Non pregnant control (n=35) No. (%)	Pregnant Woman Trimesters			Test		P-value*
		First (n=35) No. (%)	Second (n=35) No. (%)	Third (n=35) No. (%)			
Problems during this pregnancy**							
Yes	-	3 (8.6)	7 (20.0)	12 (34.3)	χ^2	5.535	0.063
No	-	32 (91.4)	28 (80.0)	23 (65.7)			
Received medication during this pregnancy							
Yes	-	5 (14.3)	3 (8.6)	5 (14.3)	χ^2	0.198	0.906
No	-	30 (85.7)	32 (91.4)	30 (85.7)			

*P-value of χ^2 (corrected) test.

P<0.05: Significant, P>0.05: Not significant.

** Problems included vaginal bleeding, infection and others.

4.4 Blood pressure of the study population

Table 4.4 indicated blood pressure of the study population. Blood pressure revealed no significant difference in systolic blood pressure among pregnant (107.6±8.3, 105.5±10.9, 108.8±11.1 mmHg in the 1st, 2nd and 3rd trimesters, respectively) and non-pregnant women (115.7±7.9 mmHg), (χ^2=2.148, P=0.098). On the hand, diastolic blood pressure recording significant decrease in pregnant women showing values of 68.3±4.6, 67.1±8.7 and 71.9±7.4 mmHg compared to 72.5±8.9 mmHg in non-pregnant women (χ^2=3.085, P=0.031).

Table (4.4): Blood pressure of the study population

Parameter	Non Pregnant Control (n=35)	Pregnant Woman Trimesters			F	P-value
		First (n=35)	Second (n=35)	Third (n=35)		
Blood pressure						
Systolic BP (mmHg)	115.7±7.9 (100-120)	107.6±8.3 (90-120)	105.5±10.9 (80-120)	108.8±11.1 (80-140)	2.148	0.098
Diastolic BP (mmHg)	72.5±8.9 (60-80)	68.3±4.6 (50-70)	67.1±8.7 (40-80)	71.9±7.4 (60-90)	3.085	0.031

P<0.05: Significant, P>0.05: Not significant.

4.5 Food intake of the study population.

Table 4.5 showed food intake of the study population. There were no significant differences in term of food intake among different groups of the study population (P>0.05).

Table (4.5): Food intake of the study population

Food intake	Non Pregnant Control (n=35) No. (%)	Pregnant Woman Trimesters			χ^2	P-value*
		First (n=35) No. (%)	Second (n=35) No. (%)	Third (n=35) No. (%)		
Fish						
Daily	1 (2.9)	0 (0)	0 (0)	1 (2.9)		
Twice/week	2 (5.7)	0 (0)	2 (5.7)	4 (11.4)	7.898	0.544
Once/week	25 (71.4)	30 (85.7)	21 (60.0)	26 (74.3)		
None	7 (20.0)	5 (14.3)	12 (34.3)	4 (11.4)		
Meat						
Daily	2 (5.7)	6 (17.1)	4 (11.4)	5 (14.3)		
Twice/week	23 (65.7)	10 (28.6)	14 (40.0)	12(34.3)	10.062	0.345
Once/week	9 (25.7)	19 (54.3)	16 (45.7)	17(48.6)		
None	1 (2.9)	0 (0)	1 (2.9)	1 (2.9)		
Egg						
Daily	10 (28.6)	14 (40)	8 (22.9)	12 (34.3)		
Twice/week	13 (37.1)	12 (34.3)	10 (28.6)	15 (42.9)	5.655	0.774
Once/week	8 (22.9)	5 (14.3)	8 (22.9)	3 (8.5)		
None	4 (11.4)	4 (11.4)	9 (25.7)	5 (14.3)		
Fruits and Vegetarian						
Daily						
Twice/week	31 (88.6)	26 (74.3)	32 (91.4)	30 (85.7)		
Once/week	3 (8.6)	7 (20.0)	1 (2.9)	2 (5.7)	5.397	0.798
None	1 (2.9)	1 (2.9)	1 (2.9)	2 (5.7)		
	0 (0)	1 (2.9)	1 (2.9)	1 (2.9)		

*P-value of $\chi^2_{(corrected)}$ test

P>0.05: Not significant.

4.6 Drink intake of the study population

Drink intake of the study population is illustrated in Table 4.6. In general, pregnant women drink less coffee, tea, soft drink and juice and more milk than non-pregnant women. The difference between the various groups was not significant except for coffee ($\chi^2_{(corrected)}$=17.313, P=0.044).

Table (4.6): Drink intake of the study population

Drink intake	Non Pregnant Control (n=35) No. (%)	Pregnant Woman Trimesters			χ^2	P-value*
		First (n=35) No. (%)	Second (n=35) No. (%)	Third (n=35) No. (%)		
Coffee						
Daily	18 (51.4)	11 (31.4)	5 (14.3)	12 (34.3)		
Twice/week	1 (2.9)	2 (5.7)	0 (0)	6 (17.1)	17.313	0.044
Once/week	4 (11.4)	6 (17.1)	10 (28.6)	4 (11.4)		
None	12 (34.3)	16 (45.7)	20 (57.1)	13 (37.1)		
Tea						
Daily	22 (62.9)	20 (57.1)	18 (51.4)	18 (51.4)		
Twice/week	6 (17.1)	2 (5.7)	1 (2.9)	6 (17.1)	6.279	0.712
Once/week	3 (8.6)	4 (11.4)	7 (20.0)	5 (14.3)		
None	4 (11.4)	9 (25.7)	9 (25.7)	6 (17.1)		
Soft drink**						
Daily	11 (31.4)	6 (17.1)	8 (22.9)	6 (17.1)		
Twice/week	6 (17.1)	2 (5.7)	5 (14.3)	10 (28.6)	7.687	0.566
Once/week	9 (25.7)	16 (45.7)	13 (37.1)	12 (34.3)		
None	9 (25.7)	11 (31.4)	9 (25.7)	7 (20.0)		
Milk						
Daily	6 (17.1)	9 (25.7)	8 (22.9)	15 (42.9)		
Twice/week	4 (11.4)	4 (11.4)	3 (8.6)	4 (11.4)	6.964	0.641
Once/week	7 (20.0)	3 (8.6)	7 (20.0)	2 (5.7)		
None	18 (51.4)	19 (54.3)	17 (48.6)	14 (40.0)		
Juice						
Daily	26 (74.3)	25 (71.4)	23 (65.7)	24 (68.6)		
Twice/week	7 (20.0)	9 (25.7)	7 (20.0)	6 (17.1)	2.154	0.988
Once/week	1 (2.9)	1 (2.9)	3 (8.6)	2 (5.7)		
None	1 (2.9)	0 (0)	2 (5.7)	3 (8.6)		

*P-value of χ^2 (corrected) test.

P<0.05: Significant, P>0.05: Not significant.

** Soft drink: Coca Cola, Sprite, Maranda,..etc.

4.7 Hemostatic parameters of the study population

Table 4.7 demonstrates hemostatic parameters include PT, INR, APTT and fibrinogen concentration. PT was significantly decreased as the pregnancy progress registering values of 10.4±0.74, 10.1±0.67 and 9.6±0.69 seconds in the 1st, 2nd and 3rd trimesters respectively (F=7.554, P=0.001). Similarly, Scheffe test showed significant decrease in PT in the 3rd trimester compared to the 1st trimester. INR showed significant decrease with values 0.86±0.08, 0.83±0.06 and 0.80±0.07 in the three trimesters respectively (F=7.576, P=0.001). However, APTT recorded no significant differences among different groups (F=1.470, P=0.225). On the other

hand, fibrinogen was significantly elevated in the three trimesters (455±17.32, 442±16.40 and 446±19.46 mg/dl) compared to non pregnant controls (294±15.78 mg/dl). F=19.894, P=0.001 (Figure 4.1).

Table (4.7): Hemostasis parameters of the study population

Parameter	Non Pregnant Control (n=35)	Pregnant Woman Trimesters			F	P-value
		First (n=35)	Second (n=35)	Third (n=35)		
PT (second)	9.8±0.68	10.4±0.74*	10.1±0.67	9.6±0.69#	7.554	0.001
Range *(min-max)*	8.40-11.10	9.00-12.00	8.80-11.60	8.70-11.30		
INR	0.80±0.05	0.86±0.08*	0.83±0.06	0.80±0.07#	7.576	0.001
Range *(min-max)*	0.72-0.91	0.71-1.00	0.74-0.92	0.72-0.95		
APTT (second)	36.4±3.5	36.4±5.1	35.9±5.0	34.4±4.6	1.470	0.225
Range *(min-max)*	30.20-45.70	27.20-49.10	27.60-49.10	25.20-44.50		
Fibrinogen (mg/dl)						
Mean±SEM	294±15.78	455±17.32*	442±16.40*	446±19.46*	19.894	0.001
Range *(min-max)*	135-580	280-610	250-608	250-612		

PT: Prothrombin Time. INR: International Normalized Ratio. APTT: Activated Partial Thromboplastin Time. All values were expressed as mean ±SD. P<0.05: Significant, P>0.05: Not significant. *compare control versus 1st, 2nd, 3rd group. # compare first versus 2nd, 3rd group.

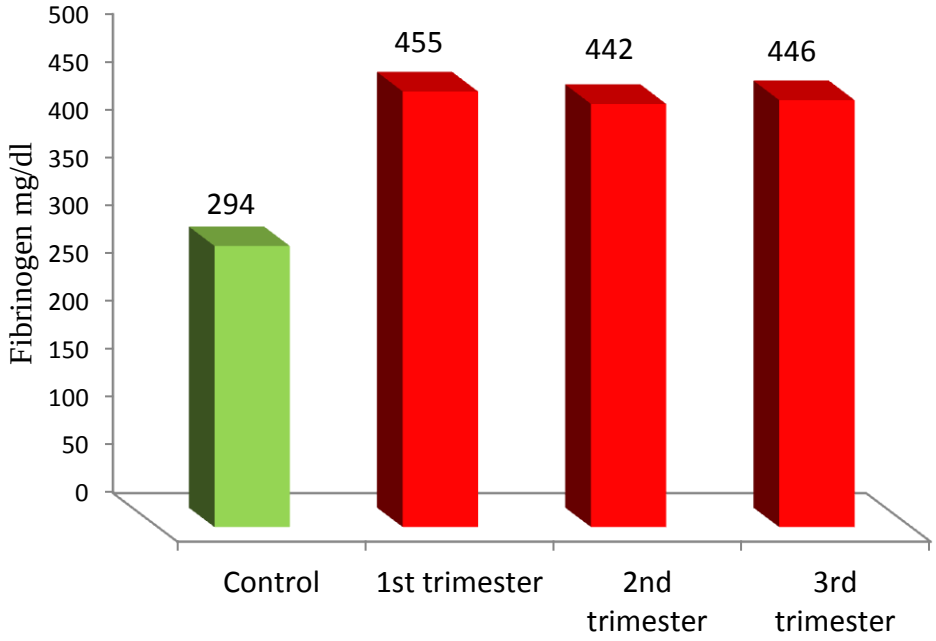

Figure (4.1): Fibrinogen concentration of the study population

4.8 Hematological parameters of the study population

4.8.1 Leukocytes

Table 4.8 illustrates the mean WBC count, lymphocytes, MID cells and granulocytes of the study population. There were significant increases in the means of WBC, MID cells and granulocyte registering the values of 7.9±2.4, 7.5±1.6 and 8.5±1.9 $\times 10^9$/L for WBC; 0.5±0.2, 0.5±0.3 and 0.7±0.3 $\times 10^9$/L for MID cells and 5.2±1.9, 5.2±1.3 and 5.8±1.6 $\times 10^9$/L for granulocyte during 1st, 2nd and 3rd trimesters of pregnancy, compared to control values of 6.7±1.6, 0.6±0.3 and 3.8±1.4 $\times 10^9$/L respectively (F=5.412, P=0.002 for WBC; F=3.074, P=0.030 for MID cells and F=9.636, P=0.001 for granulocyte). The Scheffe test showed significant increase in WBC in the 3rd trimester compared to controls. Significant increase was also found in granulocytes in the 1st, 2nd and 3rd trimesters compared to controls. Conversely, lymphocytes were generally decreased in the 1st, 2nd, and 3rd (2.2±0.7, 1.8±0.5 and 2.0±0.4 $\times 10^9$/L) compared to controls (2.3±0.5 $\times 10^9$/L), F=5.901 and P=0.001. The Scheffe test shows significant decrease in lymphocyte in the 2nd trimester compared to controls and to the 1st trimester.

Table (4.8): Leukocytes of the study population.

Parameter	Non Pregnant Control (n=35)	Pregnant Woman Trimesters			F	P-value
		First (n=35)	Second (n=35)	Third (n=35)		
WBC ($\times 10^9$/L)	6.7±1.6	7.9±2.4	7.5±1.6	8.5±1.9*		
Range *(min-max)*	3.50-9.50	4.40-12.70	3.80-10.60	4.80-14.10	5.412	0.002
Lymphocyte ($\times 10^9$/L)	2.3±0.5	2.2±0.7	1.8±0.5*#	2.0±0.4		
Range *(min-max)*	1.40-4.00	1.00-3.80	1.20-2.90	1.20-2.70	5.901	0.001
MID ($\times 10^9$/L)	0.6±0.3	0.5±0.2	0.5±0.3	0.7±0.3		
Range *(min-max)*	0.30-1.90	0.10-1.30	0.20-1.30	0.20-1.70	3.074	0.030
Granulocyte ($\times 10^9$/L)	3.8±1.4	5.2±1.9*	5.2±1.3*	5.8±1.6*		
Range *(min-max)*	1.30-6.60	1.90-8.90	2.20-8.10	2.90-11.20	9.636	0.001

WBC: White Blood Cell. MID: means mid-range absolute count. This count generally includes monocytes, eosinophils and basophils. All values were expressed as mean ±SD. P<0.05: significant. *compare control versus 1st, 2nd, 3rd group. # compare first versus 2nd, 3rd group.

4.8.2 Primary blood indices (RBC, hemoglobin and hematocrit) of the study population

The mean RBC count, hemoglobin content and hematocrit value are pointed out in table 4.9. In general, RBC and Hb showed significant decrease in the three trimesters (4.1±0.4 and 11.5±1.2 in the 1st trimester, 3.8±0.4 and 10.6±0.98 in the 2nd trimester and 3.8±0.3 and 10.9±0.95 in the 3rd trimester) compared to controls (4.2±0.3, 11.7±1.2) with F=10.612, P=0.001 for RBC and F=7.999, P=0.001 for Hb. Hct value also showed significant decrease in the three trimesters compared to controls.

Table (4.9): Primary blood indices of study population

Parameter	Non Pregnant Control (n=35)	Pregnant Woman Trimesters			F	P-value
		First (n=35)	Second (n=35)	Third (n=35)		
RBC ($\times 10^{12}$/L)	4.2±0.3	4.1±0.4	3.8±0.4*#	3.8±0.3*#	10.612	0.001
Range *(min-max)*	3.43-4.73	3.34-4.90	3.10-5.14	3.20-4.50		
Hb (g/dl)	11.7±1.2	11.5±1.2	10.6±0.98*#	10.9±0.95*	7.999	0.001
Range *(min-max)*	9.7-13.9	8.90-15.0	9.30-13.5	8.20-12.8		
Hct (%)	33.4±3.3	30.7±3.1*	30.4±2.9*	30.8±2.6*	7.652	0.001
Range *(min-max)*	27.80-40.90	23.90-36.70	25.20-36.20	25.20-36.40		

RBC: Red Blood Cell. Hb: hemoglobin content. Hct: hematocrit value. All values were expressed as mean ±SD. P<0.05: significant. *compare control versus 1st, 2nd, 3rd group. # compare first versus 2nd, 3rd group.

4.8.3 Secondary blood indices (MCV, MCH and MCHC) of the study population

Table 4.10 demonstrates secondary blood indices including MCV, MCH and MCHC. MCV increases as the pregnancy progresses. The Scheffe test showed significant increase in the 3rd trimester compared to the 1st trimester (81.8±7.5 versus 75.8±7.9). MCH exhibited no significant difference among various groups (F=1.246, P=0.296). MCHC displays significant increase in the 1st trimester with respect to controls and then significant decreases was recorded in the 2nd and 3rd trimesters compared to 1st trimester (F=9.644, P=0.001).

Table (4.10): Secondary blood indices of the study population

Parameter	Non Pregnant Control (n=35)	Pregnant Woman Trimesters			F	P-value
		First (n=35)	Second (n=35)	Third (n=35)		
MCV (fL)	80.1±6.3	75.8±7.9	79.8±7.1	81.8±7.5#	4.374	0.006
Range *(min-max)*	69.20-95.30	56.10-94.70	58.00-95.00	95.30-93.00		
MCH (pg)	28.0±2.3	28.2±2.8	27.8±2.5	28.9±2.6	1.246	0.296
Range *(min-max)*	22.60-31.70	21.10-32.50	19.8-31.80	22.10-33.90		
MCHC (g/dl)	35.0±1.7	37.4±2.9*	35.0±2.3#	35.4±1.8#	9.644	0.001
Range *(min-max)*	31.3-38.00	31.50-42.80	31.50-41.90	31.40-39.50		

MCV: Mean Cell Volume. MCH: Mean Corpuscular Hemoglobin. MCHC: Mean Corpuscular Hemoglobin Concentration. All values were expressed as mean ±SD. P<0.05: significant. *compare control versus 1st, 2nd, 3rd group. # compare first versus 2nd, 3rd group.

4.8.4 Platelets and ESR of the study population

Platelets count and ESR of the study population were provided in table 4.11. The mean platelets counts in controls, 1st, 2nd and 3rd trimesters of pregnancy were 238±62, 243±82, 199±56 and 183±72, respectively. The ANOVA test indicates significant difference among controls and three trimesters of pregnancy (F=6.247, P=0.001). The Scheffe test shows significant decrease in platelets count in the 3rd trimester compared to controls, and also significant decrease in platelets count in the 3rd trimester compared to the 1st trimester. In contrast, progressive increase was recorded for ESR toward the 3rd trimester of pregnancy (F=16.146, P=0.001). The Scheffe test revealed significant increases in ESR in 2nd, and 3rd trimesters compared to controls, and also significant increase in the 3rd trimester compared to the 1st trimester.

Table (4.11): Platelets count and ESR of the study population

Parameter	Non Pregnant Control (n=35)	Pregnant Woman Trimesters			F	P-value
		First (n=35)	Second (n=35)	Third (n=35)		
Platelets ($\times 10^{9/L}$)	238±62	243±82	199±56	183±72*#	6.247	0.001
Range *(min-max)*	161-409	80-428	108-336	81-423		
ESR (mm/1h)	17.1±18.1	24.9±15.0	37.7±21.0*	47.9±25.0*#	16.146	0.001
Range *(min-max)*	5.0-95	3.0-60	10.0-110	10.0-120		

ESR: Erythrocyte Sedimentation Rate. All values were expressed as mean ±SD. P<0.05: significant. *compare control versus 1st, 2nd, 3rd group. # compare first versus 2nd, 3rd group.

4.9 Calcium concentration of the study population

Calcium concentration of the study population is presented in table 4.12. In general, calcium concentrations were significantly lower during the three trimesters (9.18±0.6, 9.15±0.7 and 9.19±0.8 mg/dl) with respect to controls (9.65±0.5mg/dl), (F=4.839, P=0.003).

Table (4.12): Calcium level of the study population

Parameter	Non Pregnant Control (n=35)	Pregnant Woman Trimesters			F	P-value
		First (n=35)	Second (n=35)	Third (n=35)		
calcium (mg/dl)	9.65±0.5	9.18±0.6*	9.15±0.7*	9.19±0.8*	4.839	0.003
Range *(min-max)*	8.80-10.80	7.90-10.20	7.40-10.10	6.60-10.60		

All values were expressed as mean ±SD. P<0.05: significant. *compare control versus 1st, 2nd, 3rd group.

4.10 Correlation between fibrinogen concentration and other studied parameters of the study population.

Correlation between fibrinogen concentration and other parameters in both controls and pregnant women is pointed out in table 4.13 and Figure 4.2.The Pearson correlation coefficient test showed significant positive correlations of fibrinogen with WBC (r=0.427, P=0.011), Granulocyte (r=0.494, P=0.003), MCV (r=0.358, P=0.035) and ESR (r=0.340, P=0.045), and negative significant correlation with MID (r=-0.357, P=0.035) in controls. In addition, fibrinogen concentration showed

positive significant correlation with WBC (r=0.196, P=0.045), Granulocyte (r=0.219, P=0.025), and ESR (r=0.260, P=0.007) in pregnant women. On the other hand, there were no significant correlations between fibrinogen concentration and lymphocyte, RBC, hemoglobin, Hct, MCH, MCHC, platelets, PT, INR, APTT and Ca in both controls and pregnant women.

Table (4.13): Correlation between fibrinogen concentration and other studied parameters of the study population.

Parameters	Fibrinogen concentration (mg/dl)			
	Control (n=35)		Pregnant women (n=105)	
	r	P-value	R	P-value
WBC (10^9/L)	0.427	0.011	0.196	0.045
Lymphocyte (10^9/L)	0.287	0.094	-0.038	0.704
MID (10^9/L)	-0.357	0.035	0.045	0.648
Granulocyte (10^9/L)	0.494	0.003	0.219	0.025
RBC (10^{12}/L)	-0.254	0.141	0.070	0.478
Hb (g/dl)	0.070	0.691	-0.024	0.810
Hct %	0.109	0.534	-0.094	0.338
MCV (fL)	0.358	0.035	-0.147	0.133
MCH (pg)	0.300	0.079	-0.095	0.337
MCHC (g/dl)	-0.079	0.653	0.087	0.378
Platelets (10^9/L)	0.058	0.742	0.058	0.557
ESR (mm/1h)	0.340	0.045	0.260	0.007
PT (second)	0.017	0.923	0.001	0.992
INR	-0.015	0.931	0.011	0.913
APTT (second)	-0.026	0.881	-0.002	0.988
Ca (mg/dl)	0.191	0.271	0.003	0.976

The correlation was analyzed using Pearson correlation coefficient (normally distribution data).
P value significant at P<0.05

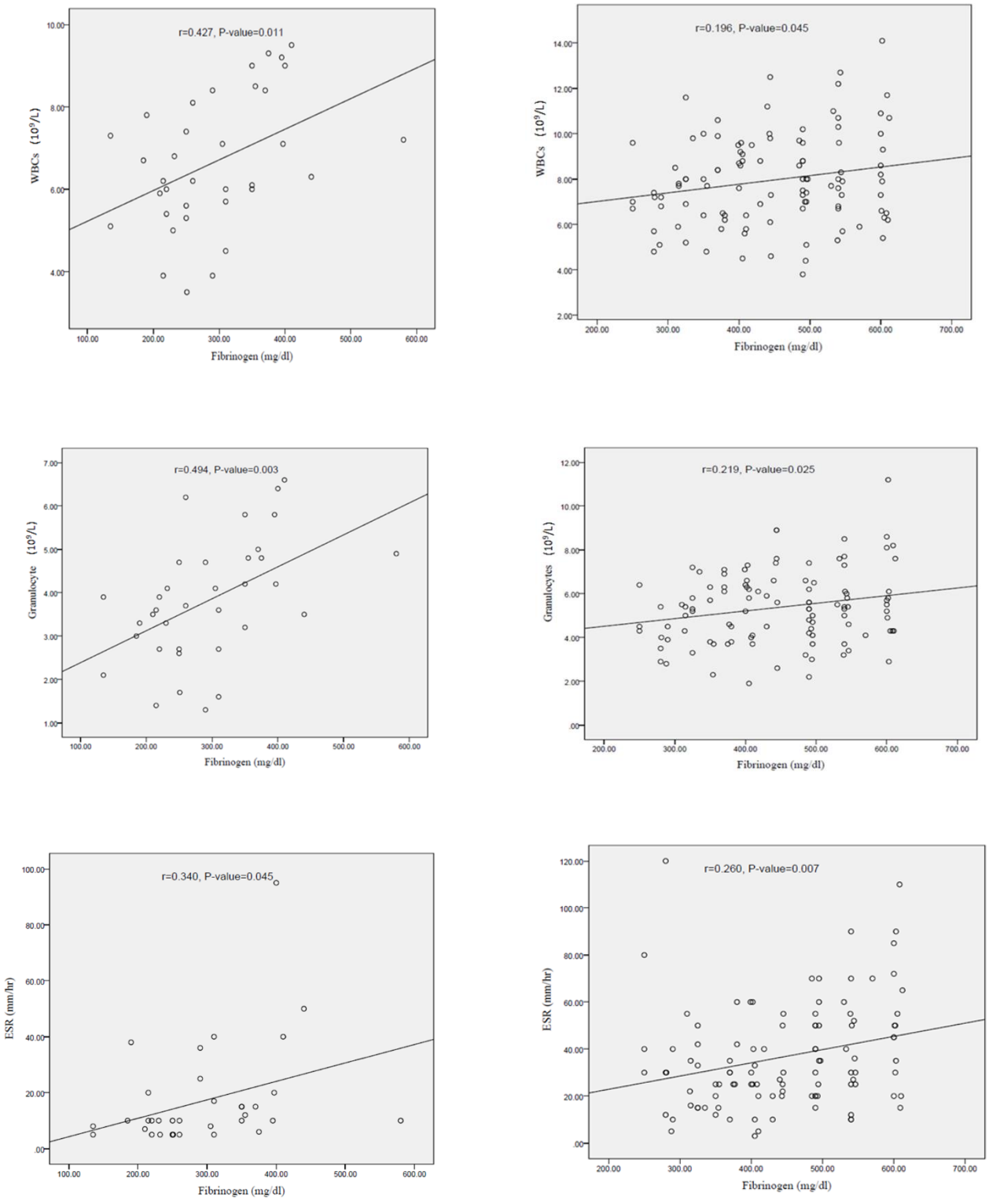

Figure (4.2): Fibrinogen concentration in relation to WBC, granulocytes and ESR in controls and cases.

Chapter 5

Discussion

Chapter 5
Discussion

Maternal mortality as well as infant mortality rates are unacceptably high. About 830 women die from pregnancy- or childbirth-related complications around the world every day. By the end of 2015, roughly 303 000 women have been died during and following pregnancy and childbirth. Between 2016 and 2030, the target is to reduce the global maternal mortality ratio to less than 70 per 100 000 live births (WHO, 2015). In Gaza strip, the mortality rate of the mother and her infant is being increased as a result of pregnancy complications. Despite that, there is under reporting of the condition, which imposes a potential burden on the health sector and on the family members in the Palestinian society. Prognostic assessment of complications accompanied pregnancy in blood testing may be of diagnostic and therapeutic values in the course of pregnancy complications. Such strategy may enable us to alleviate and/or to prevent such complications in order to protect women to have a successful pregnancy.

5.1 Sociodemographic data of the study population

Sociodemographic data of the study population presented in this study showed that higher number of pregnant women were unemployed compared to non-pregnant women. In addition, the pregnant women have lower income than non-pregnant women. These findings are in agreement with that obtained by Cleland et al. (2006); Russel and banks (2011); Rawe et al. (2012); Al-Tawil, (2013). It was reported that employed women faced a self-conflict between employment and motherhood (Baum, 2004), many employers consider pregnancy as a disadvantage in terms of low labor force participation. Rawe et al. (2012) reported that poor families often have large numbers of children, partly because they have limited or no access to contraception and they may lack knowledge on family planning.

5.2 Medical history and clinical data of the study population

Medical history of the study population showed that the frequency of the previous pregnancy in controls was higher than that in cases. Although controls have higher number of live babies than cases, yet they have higher previous pregnancy problems. The differences in term of having previous pregnancy, live baby and previous pregnancy problems were not significant between cases and controls (P> 0.05). World health organization (2012) reported that women who have more than four children are at increased risk of infant and maternal mortality. Clinical data of the study population showed that the frequency of the problems reported in the current pregnancy was increased with the progression of pregnancy. However the difference between the three trimesters was not significant (P=0.063). Similarly, no significant difference was observed among the three trimesters in term of receiving medication during pregnancy. Regarding blood pressure of the study population, both systolic and diastolic blood pressures decreased in the first and second trimesters and then improved in the third trimester with respect to that of controls. The difference in diastolic blood pressure between the various groups was significant, whereas that in systolic pressure was not significant. Similar results were obtained by Hermida et al. (2001); Al-Tawil, (2013). In normal pregnancy, it is accepted that blood pressure falls in the 1st trimester caused by active vasodilatation, achieved through the action of local mediators such as prostacyclin and nitric oxide as well as the elevated progesterone. This reduction in blood pressure primarily affects the diastolic pressure and a drop of 10 mmHg is usual by 13-20 weeks gestation. Blood pressure contentious to fall until 22-24 weeks and then gradually increases to pre-pregnancy level (James and Nelson-Piercy, 2004; Guyton and Hall, 2011).

5.3 Food and drink intake of the study population

In the present study, there were no significant differences in food intake (fish, meat, egg, fruits and vegetables) among pregnant women and controls (P>0.05). Concerning drink intake, the number of pregnant women who drink coffee was significantly less than non-pregnant women. Similar result was pointed out by Sato et al. (2010) who found that pregnant women drink coffee less frequently than non-pregnant women. On the other hand, there were no significant differences between pregnant and non-pregnant women in term of drinking tea, soft drink, milk and juice.

5.4 Hemostatic profile of the study population

Data presented in this study showed significant decreases in PT and INR as the pregnancy progress, whereas APTT showed no significant differences among controls and the three trimesters of pregnancy. Earlier studies showed reduction in maternal PT values compared to controls (Hellgren, 2003; Uchikova et al., 2005; Durotoye et al., 2012). This may be explained by the fact that the hemostatic balance tilts in the direction of hypercoagulability, which helps to reduce bleeding complications during delivery (Akinlaja, 2016). In addition, the hormones which are necessary for the maintenance of pregnancy i.e. estrogen and progesterone increase several folds and these especially estrogen stimulate hepatocyte thereby increasing the production of all coagulation factors (Durotoye et al., 2012). On the other hand, fibrinogen concentration was significantly elevated in the three trimesters compared to controls. This result is similar to that found by Hellgren, (2003); Durotoye et al. (2012); Han et al. (2014). In addition, Uchikova et al. (2005) found a tow fold increase in fibrinogen level in pregnant women compared to controls. Fibrinogen is an important factor in pregnancy as it assists in preventing post-partum hemorrhage with 5-10% of the total circulatory fibrinogen being deposited at the placental site (Hellgren, 2003). Elevation of fibrinogen levels in the three trimesters of pregnancy may be due to 1) increased ESR as observed in our results and 2) hormonal changes, especially to the increasing estrogen levels (Durotoye et al., 2012). WBC, granulocytes and ESR showed significant positive correlation with fibrinogen of the study population. This means that elevation of fibrinogen is accompanied with alteration in some blood parameters, which may alleviate pregnancy complications in term of bleeding and infections.

5.5 Hematological profile of the study population

5.5.1 Leukocytes

White blood cells, MID and granulocytes were significantly increased whereas lymphocyte count was decreased in pregnant women compared to non-pregnant women as pregnancy proceeds. Such findings are in agreement with that obtained by James et al. (2008); Osonuga et al. (2011). A pregnancy related leukocytosis with an increase in granulocytes particularly neutrophils has been seen from the

second month of pregnancy with an upward trend observed as pregnancy progress (Pramanik et al, 2007). Leukocytosis occurring during pregnancy may be due to the physiologic stress induced by the pregnant state (Chandra et al., 2012; Purohit et al., 2015). In this context, Osonuga et al. (2011) explained this change as a result of the body building the immunity of the fetus and it is achieved by a state of selective immune tolerance, immunosuppression and immunomodulation in the presence of a strong antimicrobial immunity. There is also down-regulation of potentially dangerous T-cell-mediated immune responses, while activating certain components of the innate immune system, such as neutrophils, which are the major type of leukocyte on differential count (Guyton and Hall, 2011; Akinlaja, 2016). The lymphopenia observed during pregnancy in the present study helps in preventing fetal allograft rejection. There is various changes in the immunological function, which generally leads to decreased cell mediated immunity and increased humoral or antibody mediated immunity (Redman et al, 2014). The above unique dysregulation between different components of the immune system plays a central role in the maternal adaptation to pregnancy (Akinlaja, 2016). When related to fibrinogen, WBCs and granulocytes showed significant positive correlation with fibrinogen in cases and controls, whereas MID showed significant negative correlation with fibrinogen in controls. This association may constitute a protective strategy for both mother and her fetus during pregnancy. In their review articles, Chandra et al. (2012); Costantine (2014) reported increase in both fibrinogen and WBC count as pregnancy progresses.

5.5.2 Primary and secondary blood indices

Primary blood indices including red blood cell count, hemoglobin content and hematocrit value were significantly lower in pregnant women compared to non-pregnant women. Such finding were in agreement with that obtained by Das et al. (2013); Ifeanyi et al. (2014), In addition, Verma et al. (2013) showed that Hb, RBC and Hct fall progressively from the end of the first trimester until a few weeks, before term returning to normal 1-2 months post-partum. During pregnancy, an increased plasma volume with the lack of an adequate increase in erythrocytes mass results in a decrease in hemoglobin level and the development

of anemia, which is defined as dilution anemia (Wahed et al., 2008;Ichipi-Ifukor et al., 2013). In addition, there is marked demand of extra iron during pregnancy especially in the second half (Verma et al., 2013). In such condition, Hct is expected to be lower in the pregnant women compared to controls. Thus, the fall in haemoglobin concentration during pregnancy is due to combined effect of haemodilution and negative iron balance that is due to increased demand. MCV recorded significant increments in the third trimester compared to 1^{st} and 2^{nd} trimesters of pregnancy. Chandra et al. (2012) demonstrated a small increase in MCV among the three trimesters of pregnancy and explained this change by increasing in the production of RBCs (younger RBCs and larger in size) to meet the demands of pregnancy. On the other hand, some authors found no significant change in MCV during pregnancy. In addition, MCHC showed significant decreases in the 2^{nd} and 3^{rd} trimesters compared to 1^{st} trimester. Similar results were documented by Asif et al. (2007); James et al. (2008); Chandra et al. (2012).

5.5.3 Platelets count and ESR

In general, platelet count was significantly decreased in pregnant women compared to non-pregnant women. This result is in agreement with that obtained by Akinbola et al. (2006); Ichipi-Ifukor et al. (2013), Imoru and Buseri; (2015); Purohit et al. (2015). The decrease in platelets count may be partially due to hemodilution and to increased platelet activation, consumption and accelerated clearance (Ramsay, 2010). In addition, there is an increase in Thromboxane A_2 with an increased tendency for platelets aggregation in pregnancy (Hayashi et al., 2002). Conversely, ESR was progressively increased as the pregnancy advances. Such finding is similar to that found by Osonuga et al. (2011);Das et al. (2013); Akinlaja, (2016). Elevation of ESR during pregnancy may be as a result of anemic state due to plasma expansion and decrease in packed cell volume (Manten et al., 2004). This is supported by our finding that Hct decreased significantly in pregnant women compared to controls. ESR elevation may also be due to marked increase in circulating fibrinogen in pregnancy (Verma et al., 2013), an explanation coincides with our results which showed significant increase in fibrinogen level in pregnant women compared to controls. When related to fibrinogen, ESR showed significant positive correlation with fibrinogen

in both cases and controls. It is accepted that increase of fibrinogen in the course of pregnancy is accompanied by increase in ESR (Oke et al., 2011; Krishnaveni, 2014).

5.6 Calcium concentration of the study population

The present study indicated significant decrease in Ca concentration during the three trimesters of pregnancy with respect to controls. This result is in accordance with that reported by Ritchie and King (2000); Ikechukwu et al. (2005); Hanna. (2009) and Benali and Demmouche, (2014). The observed decrease of serum calcium during pregnancy may be attributed to: 1) fetal demand of maternal calcium for bone mineralization, 2) increase transfer of ionized calcium from the mother to the fetus as pregnancy advances, 3) poor intestinal absorption of maternal calcium and 4) increase urinary calcium excretion due to normal expansion of maternal blood volume and hormonal changes (Ikechukwu et al., 2005; Indumati et al., 2011; Kovacs, 2016).

Chapter 6

Conclusions and Recommendations

Chapter 6

Conclusions and Recommendations

6.1 Conclusions

1. Unemployment and lower family income were more prevalent among pregnant women.

2. Both systolic and diastolic blood pressures decreased in the first and second trimesters and then improved in the third trimester with respect to controls. The difference in diastolic blood pressure between the various groups was significant, whereas that in systolic pressure was not significant.

3. Food and drink intake showed no significant differences between cases and controls, except coffee was drunk more frequently by non-pregnant women.

4. PT and INR were significantly deceased as the pregnancy advances, whereas fibrinogen concentration was significantly elevated in the three trimesters compared to controls.

5. White blood cells, MID and granulocytes were significantly increased whereas lymphocyte count was decreased in pregnant women compared to non-pregnant women as pregnancy proceeds.

6. Red blood cell count, hemoglobin content and hematocrit value were significantly lower in pregnant women compared to non-pregnant women.

7. MCV recorded significant increments in the third trimester compared to 1^{st} and 2^{nd} trimesters of pregnancy whereas, MCHC showed significant decrease in the 2^{nd} and 3^{rd} trimesters compared to 1^{st} trimester.

8. Platelet count was significantly decreased whereas ESR was progressively increased as the pregnancy progresses.

9. Calcium concentration was significantly decreased during pregnancy with respect to controls.

10. Fibrinogen showed significant positive correlations with WBC, granulocytes and ESR in both cases and controls.

6.2 Recommendations

1. Frequent monitoring of blood pressure throughout pregnancy.
2. The proper interpretation of hematological and hemostatic parameters help in early recognition antepartum and post-partum complications.
3. The physiological leukocytosis should always be kept in mind while using antibiotic during post-partum period so as to minimize its unnecessary use.
4. Calcium, iron and folic acid supplementation is recommended during second and third trimesters of pregnancy.
5. Further researches are needed to investigate the clotting factors and estrogen hormone concentration during the progression of pregnancy.

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Appendixes

Appendix 1

المجلس الفلسطيني للبحث الصحي

Palestinian Health Research Council

تعزيز النظام الصحي الفلسطيني من خلال مأسسة استخدام المعلومات البحثية في صنع القرار

Developing the Palestinian health system through institutionalizing the use of information in decision making

Helsinki Committee

For Ethical Approval

Date: 01/08/2016 **Number:** PHRC/HC/132/16

Name: ELHAM S. MUSALLAM **الاسم:** الهام سليم مسلم

We would like to inform you that the committee had discussed the proposal of your study about:

نفيدكم علماً بأن اللجنة قد ناقشت مقترح دراستكم حول:

Hemostatic profile of normal pregnant women in Gaza Governorates, Gaza strip

The committee has decided to approve the above mentioned research. Approval number PHRC/HC/132/16 in its meeting on 01/08/2016

و قد قررت الموافقة على البحث المذكور عاليه بالرقم والتاريخ المذكوران عاليه

Signature

Member **Member**

Chairman

Genral Conditions:-

1. Valid for 2 years from the date of approval.
2. It is necessary to notify the committee of any change in the approved study protocol.
3. The committee appreciates receiving a copy of your final research when completed.

Specific Conditions:-

E-Mail:pal.phrc@gmail.com

Gaza - Palestine غزة - فلسطين

شارع النصر - مفترق العيون

Appendix 2

Hematostatic profile of normal pregnant women in Gaza strip

Researcher for Musallam E.S

Questionnaire

Serial number:…….. Date:

Sociodemographic data

Q1. Name: …… Age: …….. Tel.No: ……

Q2. Education: ☐ University ☐ Secondary school ☐ Preparatory school ☐ Primary school ☐ Illiterate.

Q3. Employment: ☐ YES ☐ NO

Q4. Family income/month: ☐ < 1000 ☐ 1000-2000 ☐ > 2000 NIS

Medical Data

Q5. Have you pregnant before? ☐ YES ☐ NO

If yes, Abortion:…….. Live baby:……. Dead baby:……..

Q6. Previous pregnancy problems: ☐ YES ☐ NO

Clinical history

Q7. Problems during this pregnancy: ☐ YES ☐ NO

Q8. Received mediation: ☐ YES ☐ NO

Food intake and frequency

Q9.How often do you eat following food?

	Daily	twice / week	Once / Week	Non
o Fish				
o meat				
o Egg				
o Fruits & Vegetarian				

Q10. How often do you drink?

	Daily	Twice / week	Once / week	Non
o Coffee				
o Tea				
o Soft drink				
o Milk				
o Juice				

أختي الفاضلة إن هذا الاستبيان هو جزء من رسالة بحثية للمساعدة المجتمع على تقليل أعراض ومخاطر الحمل الخطر وتأكدي سيدتي إن هذه المعلومات لهذا الاستبيان لن يتم نشرها وإنما سيتم الاستفادة منها للغرض البحثي فقط

أوافق على المشاركة في البرنامج وتعبئة هذا الاستبيان الذي يتعلق بصحتي .

التوقيع : .....

التاريخ : .....

شكراً لحسن تعاونكن معنا

الباحثة / الهام سالم مسلم من كلية الدراسات العليا في الجامعة الإسلامية قسم التحاليل الطبية .